ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Magnesium Sulphate as Vasodilator

Q.—*What is the mechanism by which a 50% solution of magnesium sulphate acts as a vasodilator when injected intravenously?*

A.—The parenteral administration of even quite small amounts of magnesium sulphate causes a marked vasodilatation, and its use by this route has been recommended for the treatment of both peripheral and coronary arterial disease.[1] The mechanism of the vasodilatation has been studied by Haddy.[2] It is due to a local action of the magnesium cation on the smooth muscle of the small blood vessels causing a marked decrease in peripheral resistance. The vessels mainly affected are the precapillary arterioles.

REFERENCES
1 Browne, S. E., *Practitioner*, 1964, **192**, 791.
2 Haddy, F. J., *Circulat. Res.*, 1960, **8**, 57.

Cholestyramine and Hypercholesterolaemia

Q.—*Has oral cholestyramine any place in the treatment of hypercholesterolaemia?*

A.—Cholestyramine is an insoluble chloride salt of a basic anion exchange resin. When taken orally it exchanges chloride for bile acids (cholates) in the gut, forming an insoluble complex which is excreted in the faeces. By this means cholestyramine has a double effect on the serum lipids. Firstly, by binding bile acids, it interferes with the normal processes concerned with the absorption of dietary fats, which are therefore excreted in large amounts. Secondly, it interferes with the normal reabsorption of cholates so that there is a marked increase in their formation from cholesterol. When cholestyramine is fed both to animals and to man it causes a gradual fall in serum cholesterol over a period of about six weeks, the average fall being about 20%, but in some cases it is as high as 80%.[1]

These facts have been known for some time, but the drug has not found great favour in the treatment of hypercholesterolaemia. Its main drawback is its unpalatability. It has a pungent offensive odour, which is said to resemble dead fish. In doses of 12–16 g. a day it is used to control itching in cases of cholestatic jaundice, and many patients complain of nausea, heartburn, constipation, or diarrhoea in the early stages of treatment. Higher doses than this—up to 24 g. per day—are suggested for the treatment of hypercholesterolaemia, and in this dosage steatorrhoea can occur. It is not yet certain also whether the prolonged use of an agent of this nature will cause deficiencies of fat-soluble vitamins and other substances which require bile acids for their absorption.

Recently interest in the use of cholestyramine for the treatment of hypercholesterolaemia has been revived because of reports[2,3] that a new and more palatable preparation has become available in the U.S.A. and that it had been used with good results over a period of up to three years. It is understood, however, that this preparation has not yet received the official approval of the U.S. Food and Drug Administration, and that it is not at present available in Britain.

The existing position therefore is that cholestyramine cannot yet be recommended as a safe and effective drug for the treatment of hypercholesterolaemia but it does offer a possible line of attack which is certainly worth pursuing. Since cholestyramine does not interfere with the metabolism of cholesterol or other lipids within the body and is not absorbed, it is unlikely to have any major toxic effects.

REFERENCES
1 *J. Amer. med. Ass.*, 1966, **197**, 261.
2 *New Scientist*, 1967, **36**, 81.
3 *Int. Med. Trib.*, 1967, **2**, No. 39.

Cold Burns

Q.—*What are the immediate and the follow-up treatments for cold burns in workers who handle liquid gases?*

A.—The literature on such cold burns is scant, and there is not much experience among doctors in occupational health who look after workers who handle liquid gases. Those who have had experience have found that the gas evaporates from the skin without leaving a burn. A more dangerous type of cold burn occurs when the skin comes into contact with a cold metal pipe containing a liquid gas, since the skin tends to stick and to be torn off. Gloves are essential and are usually worn by workers in these situations.

There is no report of any injury to an eye by splash of a liquid inert low-temperature gas, such as liquid nitrogen, and in the experimental field pouring liquid nitrogen into the eyes of rabbits for two seconds caused no injury.[1] It seems, therefore, that there is no specific treatment for splashes with inert liquid gases, and probably no treatment is required. If, however, a burn did occur it should be treated as an electric burn with immediate skin grafting, and the Chepstow Hospital Burns Unit green-dye intravenous-injection technique[2] could be used for delineating the area which would need to be grafted.

REFERENCES
1 Grant, W. M., *J. Amer. med. Ass.*, 1964, 188, 769.
2 Tempest, M. N., *Trans. Ass. industr. med. Offrs*, 1961, **11**, 22.

Reducing Weight While Training

Q.—*Is it possible without detriment to health to reduce weight by limiting calorie intake in a growing boy who is undergoing severe training for championship swimming? Coaches have stated that shedding fat would improve performance. They also claim that vitamin supplements (particularly B, C, and E) improve performance. Is that correct?*

A.—It is possible to reduce weight by limiting calorie intake in a growing boy without detriment to health, but it would be wise to attempt this only *before* the period of training starts.

How much weight reduction is attempted should depend on this boy's height, weight, skinfold measurements, and the event for which he is training. There is great physical variation, and if the physique of cross-channel swimmers is compared with that of short- or middle-distance swimmers it seems clear that individual constitutions are better adapted to particular events (an anthropometric study of forthcoming Olympic swimmers might help to place this on a firmer scientific basis). During training the boy's diet should be mixed, with more emphasis on milk and meat than on carbohydrate. It should have sufficient calories to prevent him feeling hungry after meals.

There is no scientific basis for the statement that supplementary vitamins of the B complex, vitamin C, or vitamin E improve performance.

Congenital Abnormalities

Q.—*A couple with no family history on either side of congenital abnormalities have had one child with bilateral congenital dislocation of the hips, and a second, who lived two hours, with a cardiac abnormality and transposition of the great vessels. What is the likelihood of abnormalities in any subsequent children?*

A.—The two malformations in this family are quite independent, and the risks of recurrence are also separate and independent. If the child with congenital dislocation of the hip is a girl the risk of recurrence is about 3%.[1] The risk of recurrence of the cardiac anomaly, most likely Fallot's tetralogy, is also of this order.[2,3]

REFERENCES
1 Carter, C. O., *Progr. med. Genet.*, 1965, **4**, 59.
2 Lamy, M., De Grouchy, J., and Schweisguth, O., *Amer. J. hum. Genet.*, 1957, **9**, 17.
3 Polani, P. E., and Campbell, M., *Ann. hum. Genet.*, 1955, **19**, 209.

Shampoo Hazard

Q.—*Is there a carcinogenic hazard in using hair shampoos containing 0.15% trichlorcarbanilide (trichlorban)?*

A.—Trichlorcarbanilide is used as a bacteriostatic agent. Carbanilide (1,3-diphenylurea) is not closely related chemically to any known carcinogen and there is certainly no reason to believe that its use in shampoos involves any carcinogenic hazard.

Triple Vaccine

Q.—*For how many years has the combined triple vaccine of diphtheria, whooping-cough, and tetanus been used? My main concern is whether the tetanus toxoid was added to the other two some 15 years ago and was in general use.*

A.—The first combined antigens to be extensively used in the United Kingdom and elsewhere for routine administration against whooping-cough and diphtheria were undoubtedly mixtures of only the two components diphtheria toxoid and pertussis vaccine. The history of these "double"

antigens is well given in the report of a trial published in 1950.[1] The story goes back to 1940 or even earlier.

The "triple" antigen proper, in which tetanus toxoid was added to the other two, was probably first used in this country about 1951. It is associated with the names of Holt (then working at the Wright-Fleming Institute) and Bousfield, who did not, however, publish the results of their work until 1957.[2] Triple vaccine may have been used in other countries, particularly Canada and the U.S.A., before 1951.

By 1953 the triple vaccine was certainly available from sources other than the Wright-Fleming Institute. Glaxo Laboratories, for example, started to manufacture it in August 1953. It was in general use by 1953, though its efficiency against whooping-cough was not proved by the Medical Research Council until about 1955. The Medical Research Council, which carried out the field trials on immunization against whooping-cough,[3-5] used either single pertussis vaccines or the double vaccine of diphtheria toxoid plus pertussis vaccine. The Medical Research Council has never carried out a field trial with triple vaccine.

REFERENCES

1 Breen, G. E., Benjamin, B., and Beck, A., *Lancet*, 1950, **1**, 198.
2 Bousfield, G., and Holt, L. B., *Brit. med. J.*, 1957, **2**, 1213.
3 *Brit. med. J.*, 1951, **1**, 1463.
4 *Brit. med. J.*, 1956, **2**, 454.
5 *Brit. med. J.*, 1959, **1**, 994.

Diet and Lifespan

Q.—*What experiments on rodents, referred to in a recent leading article,[1] have indicated that the "clock" of the lifespan can be considerably slowed by simple calorie restriction?*

A.—Dietary retardation of mortality was originally described by McCay[2] in rats kept on a severely restricted calorie intake and subsequently permitted to grow. The measures adopted in this series of experiments were heroic, but much less severe degrees of calorie restriction or of intermittent fasting, insufficient to delay the onset of sexual maturity, can increase lifespan in some rat and mouse strains by 50% or more.[3-5] In some series there has been marked postponement or abolition of tumour incidence.[6]

Whether these effects represent a retardation of ageing is arguable—the postponement of most but not all senile changes is marked, and other characters (collagen contractility[7] and latent period of explanted cells in culture[8]) are said to retain the pattern of youth. The subject has been reviewed in detail.[9 10]

REFERENCES

1 *Brit. med. J.*, 1967, **3**, 814.
2 McCay, C. M. Sperling, G., and Barnes, L. L., *Arch. Biochem.*, 1943, **2**, 469.
3 Carlson, A. J., and Hoelzel, F., *J. Nutr.*, 1946, **31**, 363.
4 Berg, B. N., and Simms, H. S., *J. Nutr.*, 1960, **71**, 255.
5 Riesen, W. H., Herbst, E. J., Walliker, C., and Elvehjem, C. A., *Amer. J. Physiol.*, 1941, **148**, 614.
6 Tannebaum, A., *Ann. N.Y. Acad. Sci.*, 1947, **49**, 5.
7 Chvapil, M., and Hrůza, Z., *Gerontologia (Basel)*, 1959, **3**, 241.
8 Holečková, E., Poupa, O., and Fábry, P., *Physiol. bohemoslov.*, 1959, **8**, 15.
9 Silberberg, M., and Silberberg, R., *Physiol. Rev.*, 1955, **35**, 347.
10 Comfort, A., *Proc. Nutr. Soc.*, 1960, **19**, 125.

Notes and Comments

Sodium Cyclamate as Sweetener.—Miss SUSAN KNIBBS (Welfare Secretary, British Diabetic Association, London W.C.1) writes: With reference to the answer to this question ("Any Questions?" 20 January, p. 167), there has recently been some doubt thrown on the toxic effects of this substance in man, and the medical advisory committee of the British Diabetic Association issued a statement from which the following is an extract:

"Until recently it was thought that cyclamate was completely inert. . . . Research work reported earlier this year, however, indicated that some people taking cyclamate excrete a proportion of it in the urine as cyclohexylamine. It has been suggested that this breakdown product may have unwanted effects, though no example of this has been reported. Apart from a slight laxative effect in some people and a small number of reports of skin sensitivity, no adverse effects clearly attributable to eating cyclamate have been published. Although the risk is small, the medical advisory committee of the British Diabetic Association felt that a statement of the present position would be helpful, as diabetics as a group are particularly likely to eat foods flavoured with artificial sweeteners. If the daily consumption of cyclamate is kept below the recommended maximum of about 3 g. for an adult and proportionately less for a child it seems very unlikely that any harm can result, though until further information is available it would be wise not to take cyclamate during pregnancy. Manufacturers are required by law to state that an artificial sweetener has been added to food, but they are not compelled to say what it is nor how much has been added. The association is urging the manufacturers involved to print full information on the label. Further information about the effects of cyclamate is being sought by the association and any new developments will be published in *Balance*."

Dr. E. S. BENJAMIN (Cape Town, South Africa) writes: In connexion with the question of toxic effects of sodium cyclamate ("Any Questions?" 20 January, p. 167) S. I. Lamberg[1] reported a case of photosensitivity due to calcium cyclamate. The patient was a Negro woman who used this substance as a sweetening agent. He mentioned that similar cases had been reported from Japan. This admittedly was not a toxic effect but an example of photoallergy. The reasons given by the author for concluding that photoallergy was the probable mechanism of photosensitivity in this case were as follows: (1) The incidence of sensitivity to cyclamate in the general population is very low; (2) the minimal erythema dose of ultraviolet radiation was not decreased; (3) the control patient was not affected by the same high dose of cyclamate; and (4) the patient experienced a prolonged skin reaction with urtication, papulation, and eczematization after light exposure.

OUR EXPERT replies: I am grateful to Dr. Benjamin for drawing my attention to this report. Though cyclamates seem to be safe when taken in normal quantities, their increasing use should alert doctors to side-effects which may be due to sensitivity rather than to toxicity.

REFERENCE

1 Lamberg, S. I., *J. Amer. med. Ass.*, 1967, **201**, 747.

Non-barbiturate Hypnotics with Antidepressants.—Dr. J. G. HENDERSON and colleagues (Ross Clinic, Aberdeen) write: We were interested in the answer to the question on the use of non-barbiturate hypnotics in patients already receiving antidepressant drugs ("Any Questions?" 6 January, p. 40). Your expert's reply stimulated us to analyse our experience with a group of 49 patients with an age range of 22 to 75 suffering from varied psychiatric illnesses, all of whom received a combination of an oral antidepressant (amitriptyline) and one or more of the diazepine group of drugs (see Table).

Chlordiazepoxide, diazepam, and oxazepam were prescribed for their effectiveness in reducing anxiety symptoms. Nitrazepam was used as a sedative at night in a dosage of 5 to 10 mg., and in eight patients had been given 30 minutes after thioridazine 25 to 75 mg. This last combination, in our experience, has been an effective form of sedation for patients who, in their depressed state, have difficulty in returning to their usual sleep pattern.

In the series of 49 patients reported postural hypotension appeared only in one woman aged 68, who had received a combination of amitriptyline with nitrazepam as a sedative. The postural hypotension settled on terminating the amitriptyline. No other side-effects were noted or reported in any patient on varying combinations of drugs as outlined in the Table.

It should be noted that a number of the 49 patients received a course of electric convulsion therapy in addition to amitriptyline and drugs of the diazepine group without untoward reactions. Patients were anaesthetized without difficulty using methohexitone sodium, and, as a relaxant, suxamethonium chloride. In summary, combinations of amitriptyline and drugs of the diazepine group (including a hypnotic) were prescribed without serious side-effects.

OUR EXPERT replies: I find the results obtained by Dr. Henderson and his colleagues most interesting, but of the drugs which they administered along with the antidepressant amitriptyline only nitrazepam can be regarded as a hypnotic. Therefore their findings, except in respect of those patients who received nitrazepam, are not relevant to the original question.

Narcolepsy and Disseminated Sclerosis.—Dr. W. G. BRADLEY (Muscular Dystrophy Group Research Laboratories, Newcastle General Hospital, Newcastle upon Tyne 4) writes: Your expert who answered this question ("Any Questions?" 10 February, p. 365) may not have been aware of the report by Berg and Hanley[1] in which they described narcolepsy occurring in two patients with multiple sclerosis, the narcolepsy preceding the multiple sclerosis for eight and two years respectively.

OUR EXPERT replies: I was unaware of this case report. I do not think it affects the sense of my reply, though it suggests that narcolepsy may be a premonitory symptom of multiple sclerosis as well as a feature of the established disease.

REFERENCE

1 Berg, O., and Hanley, J., *Acta neurol. scand.*, 1963, **39**, 252.

Drugs and Combinations of Drugs Given to 49 Patients Receiving Amitriptyline

	AC	AD	AN	AO	AT	ACN	ADN	ATN	ATND	Total No. of Patients
No. of patients	1	6	13	1	1	2	16	8	1	49

Drug code and average daily dosage. A = amitriptyline 75 mg.; C = chlordiazepoxide 30 mg.; D = diazepam 15 mg.; N = nitrazepam 10 mg.; O = oxazepam 30 mg.; T = thioridazine 50 mg.